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(54) A composition for the topical treatment of acne

(57) A composition for the topical treatment of acne comprises as active ingredients are a micronized peroxide of an organic acid e.g. benzoyl peroxide and lauroyl peroxide erythromycin or a derivative thereof.

A two-part composition has the erythromycin compound in one part and the remaining ingredients in a second part. Also, described is a package having two closable containers, one containing the said erythromycin compound and the other containing the remaining ingredients.

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Fig. 1

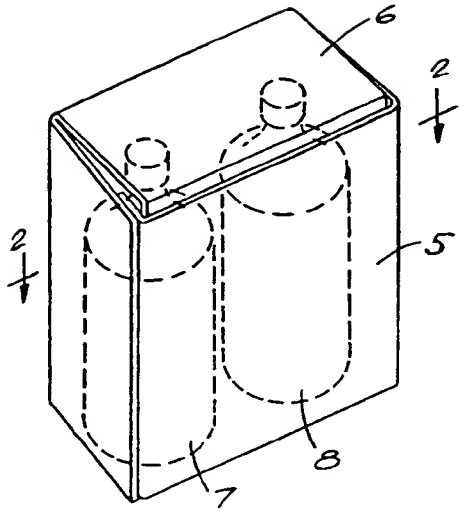


Fig. 2

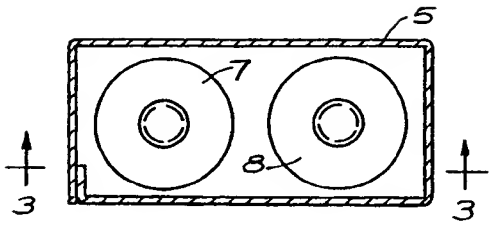


Fig. 3

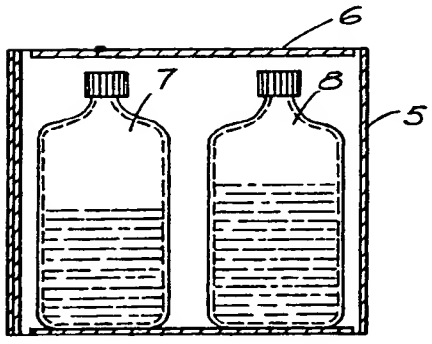
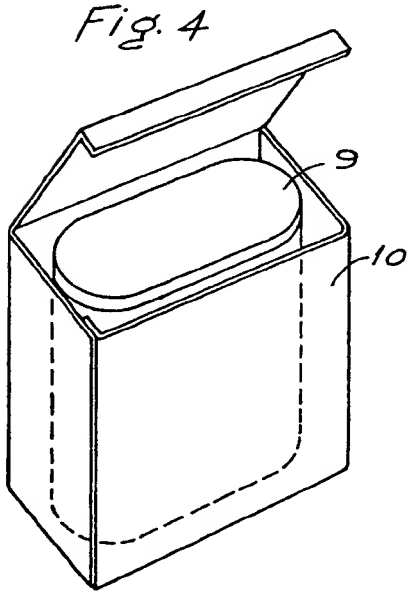


Fig. 4



SPECIFICATION

A composition for the topical treatment of acn

The present invention relates to a composition which is useful for the topical treatment of acne.

Acne is a common inflammatory disease in skin areas where sebaceous glands are largest, most numerous, and most active. In its milder types it is a more or less superficial disorder which is evidenced by slight, spotty irritations and ordinary skin hygiene is a satisfactory treatment. However, in the more inflammatory types of acne, bacterial invasion of or about the pilosebaceous follicles occurs and pustules, infected cysts and, in extreme cases, canalizing inflamed and infected sacs appear. These lesions may become extensive and leave permanent, disfiguring scars.

Acne is very common at puberty and at least 80% of teenagers are afflicted. The facial eruptions are known to cause such psychic trauma in many adolescents that they find it difficult to make personal adjustments and consequently, withdrawal and self-pity occur. The sufferer may be constantly aware of the obvious facial blemishes. For these reasons a medical treatment is of definite benefit and may eliminate the need for psychotherapy.

To reduce the severity of acne, various forms of medication have previously been applied topically to the skin. Antibacterial soaps have been used as well as bactericidal agents such as sulphur and resorcinol. Other topical compositions have separately contained benzoyl peroxide, hexachlorophene, erythromycin or neomycin sulphate. None of these prior preparations has been completely effective.

Thus, for example, U.S. Patent Specification No. 3,535,422 discloses a therapeutic composition for the treatment of acne comprising a uniform dispersion of benzoyl peroxide in a fluid medium containing water and at least one organic emollient.

In addition, U.S. Patent Specification No. 4,056,611 discloses a therapeutic composition for the treatment of acne comprising a stable dispersion of finely divided particles of benzoyl peroxide in an aqueous alcohol vehicle having a single phase. The single phase of the composition is non-lipid and contains a non-ionic surface active agent that is soluble in the aqueous alcohol vehicle.

Further in co-pending Application No. 80–24458 (Serial No. 2,054,375A), which is incorporated herein by reference, there is described and claimed the use of dioctyl sodium sulphosuccinate as a stabilizing agent for benzoyl peroxide formulations and the increased stability of benzoyl peroxide in micronized form.

Prior art peroxide compositions which contain merely finely divided peroxide particles in an emulsion of water and certain select emollients exhibit the disadvantage that when applied to the skin the water content of the emulsion evaporates, and there remains on the surface of the skin near and in contact with the acne sites most of the oraganic emollients and the large benzoyl peroxide particles, which may cause irritation.

Additionally, the use of large amounts of non-ionic surface active agents in such compositions, unless extremely fine particles of peroxide are utilized, can cause a likelihood of irritation from the peroxide.

Also, because of the powerful oxidizing properties of the peroxide component, the inclusion of this substance in a conventional ointment or emulsion or with other active ingredients results in unstable compositions that soon display an unacceptable loss in keratolytic potency.

We have now found surprisingly that a mixture on the skin of a micronized peroxide of an organic acid, especially benzoyl peroxide, and erythromycin or a derivative thereof is particularly beneficial and that together these active ingredients exert a statistically significant synergistic effect.

Accordingly, in one aspect the present invention provides a composition for the topical treatment of acne, which composition comprises, as active ingredients, a peroxide of an organic acid in a micronized form and an erythromycin compound which is erythromycin or a derivative thereof, the peroxide being present in an amount of from about one-half to about thirty times by weight of the erythromycin compound.

In the present invention, benzoyl peroxide inhibits the formation of free fatty acids in the skin, primarily through inactivation of extracellular lipase (via oxidation), lipase being necessary to cleave triglycerides into free fatty acids and glycerol. Erythromycin effectively reduces the concentration of *Corynebacterium acnes* (i.e., P. acnes), a normal anaerobic bacterium which is the prime source of the lipase. Instead of the benzoyl peroxide, which is preferred, other peroxides of organic acids may be used such as lauroyl peroxide. Instead of erythromycin, which is preferred, erythromycin derivatives may be used such as erythromycin stearate or glucoheptonate.

The two active ingredients may be applied to the skin as a mixture or they may be applied to the skin separately. In the latter practice the erythromycin is preferably applied to the skin first and immediately or shortly thereafter the peroxide is applied. However, the order of application

may be reversed if desired. If a mixture is to be made up first and then applied to the skin it is best that the mixture should be made at the time of application or that the mixture should be used within twenty-four hours. Our recommendation for prompt use of a premix is based on the relative incompatibility of the two active agents, and becaus of this it is advisable that the two agents should be stored in separate vials, bottles or other containers.

In accordance with the above, the invention in another aspect provides a two-part composition for the topical treatment of acne, which composition comprises: in a first part an erythromycin compound which is erythromycin or a derivative thereof, and in a second part an organic acid peroxide in a micronized form and a pharmaceutically-acceptable diluent or carrier, the peroxide and the erythromycin compound being provided in a ratio whereby when the two parts are mixed the peroxide is present in an amount of from about one-half to about thirty times by weight of the erythromycin compound.

Furthermore, the invention also provides a package for providing a composition according to the invention, which package comprises a first closable container having therein a said erythromycin compound and optionally a solvent therefor, and second closable container having therein a said organic acid peroxide together with any additional ingredients, the package including means to indicate or ensure that the contents of the containers are mixed in a ratio such that in the resulting mixture the amount of peroxide is from about one-half to about thirty times by weight of the erythromycin compound.

As a still further feature of the present invention there is provided a vehicle for the active ingredients whereby the mixture of the ingredients is provided with a surprising stability and shelf life at temperatures conventionally employed for the storage of erythromycin solutions; additionally, the vehicle provides a more uniform dispersion of active ingredients. Thus, it has been found surprisingly that in an aqueous alcoholic gel vehicle the utilization of a micronized peroxide and an erythromycin compound in combination with dioctyl sodium sulphosuccinate as the surface active agent results in a composition which displays full stability with respect to the peroxide component even when subjected to temperatures higher than those normally expected in the ordinary use of the product. Also, the mixture of the present invention upon evaporation allows a uniform release of the peroxide so as to obviate the burning and erythema experienced with other harsh formulations.

The therapeutic gel composition of the present invention should contain sufficient peroxide to be therapeutically effective, and should not contain more peroxide than can be uniformly dispersed in the chosen vehicle to form, for example, a smoothly spreadable composition. Such considerations dictate that the composition generally may contain at least about 1% and not more than about 30% by weight of peroxide, and preferably the composition contains from about 2.5% to about 15% by weight of peroxide, more preferably from 5% to 15% by weight. The peroxide constituent of the composition should be of high purity and generally in the form of micronized particles, the finely divided crystalline particles preferably having a mean average particle size of less than about 35 microns, and especially in the case of benzoyl peroxide typically a size less than about 150 microns. Utilizing a peroxide which has been micronized provides greater stability and shelf life to the composition, especially when used in combination with dioctyl sodium sulphosuccinate as the surfactant.

Dioctyl sodium sulphosuccinate which serves as a surface active agent as well as providing for the increased stability of the composition may be present in an amount of from about 0.1% to about 6%, preferably about 0.1% to about 2%, by weight of the composition. The composition may also advantageously contain a further wetting agent in an amount of from about 1.0% to about 6.0% by weight and preferably from about 3% to about 6% by weight. As a further wetting agent there may be used, for example, esters of polyols and sugars, the products of the condensation of ethylene oxide with fatty acids, fatty alcohols, long-chain alkyl phenols, long-chain mercaptans, long-chain amides, polyethers of polyhydroxylated fatty alcohols and alkyl polyglycol ethers.

In the description which follows reference is made to the accompanying drawings in which:

Figure 1 is a perspective view of a package containing two containers, one for each active ingredient;

Figure 2 is a section on the line 2–2 of Fig. 1;

Figure 3 is a section on the line 3–3 of Fig. 2; and

Figure 4 is a perspective view of a package containing a single jar.

A mixture of the two active ingredients may be lightly dusted on the affected skin area much in the same manner that ordinary face powder may be applied. This may be an application of ith r a premix from a container as shown in Fig. 4, or of successively applied active ingredients from two containers as shown in Figs. 1 to 3, or of a premix from two such containers made at the time of application.

In addition, it is possible to dilute the peroxide ingredient or the mixture of ingredients with a pharmaceutically-acceptable diluent or carrier which may be a solid such as a powder, a semi-solid vehicle of creamlike consistency or a liquid such as a water, to provide an emulsion, or an

organic solvent, to provide a solution. Especially preferred is an aqueous mixture containing dioctyl sodium sulphosuccinate as a surfactant.

On a weight basis, the selected erythromycin and the selected peroxide should be measured out so that as applied to the skin the latter is preferably from about one to about thirty times the weight of the former, more preferably from about one to about five times. In a premix composition including a diluent or carrier the selected erythromycin should preferably be present at a level ranging from about 0.5% to about 5.0% w/w and the selected peroxide should preferably be present at a level ranging from about 1% to about 30% w/w. More preferred levels are from about 2% to about 3% for the selected erythromycin and from about 5% to about 10% for the selected peroxide.

Since erythromycin is limited in its solubility, the preferred dermatologic solvents are alcohol or acetone but the composition is not limited to the use of these liquids. In solution, erythromycin rapidly degrades, even at ambient temperature. Refrigeration, however, can extend the shelf-life of such solutions somewhat.

A preferred diluent or carrier is a hydroalcoholic gel system, but liquid suspensions and emulsions, as well as creams, ointments and powders are acceptable. Conventional pharmaceutical processes may be used in making up these common forms of medicinal topical compositions. For instance, a premix may be place in a capped conventional ointment or like container 9 as shown in Fig. 4 as this would minimize the stability problem. The patient should instructed to refrigerate the preparation. Ordinarily, the jar 9 would be in a cardboard or like package 10.

For a commercial preparation it is best to make up a cardboard package 5 with a cover 6, which includes two capped containers as is shown in Figs. 1 to 3. One container has only the erythromycin in it and is large enough to accommodate all the other ingredients later to be mixed with the erythromycin. The other container contains an aqueous gel benzoyl peroxide composition, with or without a solvent for the erythromycin, as well as the other ingredients to make up the topical composition.

The gelling agent used in this invention may be selected both as to type and quantity to give products of various viscosities. In the preferred form of this invention, the gelling agent is selected so as to produce an elegantly formed and stable gel. A variety of gelling agents may be used for the present purposes and preferred gelling agents are pure micro-crystalline cellulose, colloidal magnesium aluminium silicate, hydroxypropyl methyl cellulose and the so-called hydroxylated vinylic polymers, particularly, those disclosed in U.S. Patent Specification No. 2,798,053. Among hydroxylated vinylic polymers of special interest herein are those described generally as interpolymers of a monomeric monoolefinic acrylic acid, and from about 0.1% to about 10% by weight based on the total monomer of a monomeric polyether of an oligosaccharide in which the hydroxyl groups which are modified are esterified with allyl groups, said polyether containing at least two ether groups per oligosaccharide molecule. Commercially available interpolymers of this type are marketed under the name Carbopol (registered Trade Mark). These are described as being polymers of acrylic acid cross-linked with about 1% of a polyallyl ether of sucrose having an average of about 5.8 allyl groups for each sucrose molecule. These polymers have molecular weights of an order of magnitude of about 1,000,000. Such polymers are available from the B. F. Goodrich Chemical Company and are sold under such trade names as Carbopol 934, Carbopol 940, and Carbopol 941.

The quantity of gelling agent that may be contained in the present compositions may also vary somewhat. Generally, the gelling agent may constitute from about 0.1% to about 15% by weight, and preferably from about 0.5% to about 3% by weight, based on the total weight of the finished composition.

As mentioned above, the simplest topical preparation is a mixture of micronized benzoyl peroxide and erythromycin with no diluent, but it would have to be sparingly applied to the skin. Instead of applying a premixture of both active ingredients one ingredient may be applied to the skin first and then the other ingredient applied with a slight rubbing action to mix the ingredients on the skin.

The following Examples illustrate the invention, but are not to be taken as limiting the invention. In each of the Examples the micronized peroxide used is one having a particle size of less than about 150 microns and a mean average particle size of less than about 35 microns.

Example 1

A simple preparation is the following:

Benzoyl peroxide (micronized)	1 to 35% w/w
Calcium phosphate	63 to 98.5% w/w
Erythromycin	0.5 to 5% w/w

The above ingr dients are intimately mixed together and dusted on the affected skin area, from one to four times daily. The preparation may be sold in the container 9 of Fig. 4.

Example 2

If a liquid preparation is desired, the following is a simple composition which may be made and applied to the skin from one to four times daily as though it were an ordinary face lotion. It may be sold in one of the bottles of Fig. 1 with or without the carton 5.

Ethanol	Q.S. to 100% w/w
Erythromycin	0.5 to 5% w/w
Benzoyl peroxide (micronized)	1 to 30% w/w

Example 3

A Lotion

In a first container such as 7 are placed the following ingredients, by weight:

	100%
Ethoxylated cetyl-stearyl alcohol	7.00%
Cetyl alcohol	0.75%
Isopropyl myristate	5.00%
Butylated hydroxyanisole	0.10%
Polyoxyl 40 stearate	0.25%
Water, deionized or distilled	68.80%
Propylene glycol	3.00%
Benzoyl peroxide (micronized)	5.00%
Acetone	10.00%
Dioctyl sodium sulphosuccinate	0.10%

In a second container such as 8 is placed the following ingredient by itself, the container being large enough to accommodate a quantity of a solvent, preferably, ethanol or acetone, in a ratio of 3 cc/20 grams of the composition in container 7.

Erythromycin	2% w/w of the contents of container 7

Both containers are put in a single marketable package such as 5 with the instructions that the contents of container 8 are to be added to container 7 and thoroughly mixed. Alternatively, to container 8 having the erythromycin is added 3 cc. of ethanol per each 20 grams of material in container 7. The solution of erythromycin in ethanol is then added to container 7 and thoroughly mixed. This would either be done by the pharmacist or by the patient. The patient would apply the lotion to the skin as though it were an ordinary lotion from one to four times daily.

A variation of Example 3 is to dilute the erythromycin of container 8 with the same solvent whereby some of the contents of container 7 may be applied to the skin first and then some of the contents of container 8 so that the mixture occurs on the skin. This eliminates loss of activity due to storage of the mixture.

Example 4

A Cream

In a first container such as 7 are placed the following ingredients, by weight:

Ethoxylated cetyl-stearyl alcohol	15.00%
Cetyl alcohol	1.25%
Isopropyl myristate	5.00%
Butylated hydroxyanisole	0.10%
Polyoxyl 40 stearate	0.25%
Water, deionized or distilled	60.30%
Propylene glycol	3.00%
Benzoyl peroxide (micronized)	5.00%
Acetone	10.00%
Dioctyl sodium sulphosuccinate	0.10%

In a second container such as 8 is placed the following ingredient by itself, the container being large enough to accommodate a quantity of a solvent, preferably, ethanol or acetone, in the ratio of 3 cc./20 grams of the composition in container 7.

Erythromycin	3% w/w of the contents of container 7.

The instructions for sale and use in Example 3 apply equally to this cream. Since the preparation is of cream consistency the containers 7 and 8 should have wide mouths to facilitate mixing and removal of the cream.

Example 5.

A Gel

A first container such as 7 has in it the following ingredients, by weight:

Water, deionized or distilled	54.65%
Colloidal Bentonite	2.50
Carboxy vinyl polymer (acid form)	1.00%
Dioctyl sodium sulphosuccinate	1.00%
Diisopropanolamine	0.75%
Ethyl alcohol, 200°	35.00%
Butylated hydroxyanisole	0.10%
Benzoyl peroxide (micronized)	5.00%

A second container such as 8 has in it only the following:

Erythromycin	3% w/w of the contents of container 7.

The instructions for packaging in wide mouth containers, and compounding at the time of dispensing in Example 4 apply to this gel.

Example 6.

A suspension

A first container such as 7 has in it the following ingredients, by weight:

Water, deionized or distilled	56.97%
Colloidal Bentonite	1.50%
Carboxyl vinyl polymer (acid form)	0.25%
Dioctyl sodium sulphosuccinate	1.00%
Diisopropanolamine	0.18%
Ethyl alcohol, 200°	35.00%
Butylated hydroxyanisole	0.10%
Benzoyl peroxide (micronized)	5.00%

Container 8 has in it only the following:

Erythromycin	2% w/w of the contents of container 7

The instructions for use in Example 3 apply to this suspension.

In any of the above Examples 3 to 6, the amount of benzoyl peroxide may be reduced or increased within the range of from 1% to 30% w/w of the contents of container 7, the amount of water being proportionately increased or reduced. The amount of erythromycin in container 8 should be measured to amount of one-fifth to two times w/w of amount of benzoyl peroxide employed.

In any of the above Examples another organic acid peroxide may be substituted for the benzoyl peroxide.

In any of Examples 3 to 6, water may be substituted for acetone and/or a lower alkanol such as methanol or ethanol may be used. The use of acetone or alcohol may also be changed depending on th wishes of th artisan.

In any of th above Examples an erythromycin derivative may be substituted for the erythromycin.

Thus, the above Examples are illustrations of this invention and are not to be construed as limitations thereof. It is to be understood that certain of the above ingredients may be replaced by other ingredients which ar well known to the skill d artisan in dermatological preparations.

Varying amounts of other ingredients or alternative excipients may be added or interchanged as the artisan sees pits and falls within the meaning of this invention.

Example 7

(A) 495.0 mg of purified water were stirr d and 15.0 mg of Carbopol 940 (carboxyl vinyl polymer, acid form, of B.F. Goodrich Co.) were add d to the water while stirring. Stirring of the mixture was continued for 45 minutes. Then 4.095 mg of sodium hydroxide in 4.91 ml of purified water were added thereto. Stirring of the mixture was continued for 10 minutes, whereupon 150.0 mg of ethyl alcohol, 0.50 mg of perfume and 0.50 mg of methyl salicylate were added. To the stirred mixture was then added a mixture comprising 210.0 mg of wet pack micronized benzoyl peroxide (50% benzoyl peroxide— 50% water), 2.0 mg of dioctyl sodium sulphosuccinate, 41.0 mg of alkyl polyglycol ether and 41.0 mg of purified water. The mixture was stirred for 30 more minutes until a smooth and elegant gel mixture was obtained.

(B) Three samples of the gel formulation from Part A weighing approximately 20.0 gm were mixed with 0.8 gm of Erythromycin in 3.0 ml abs. EtOH to yield a total weight of 23.25 gm. Each gram of sample contained 34.40 mg of Erythromycin.

On the initial day of the experiment (0 time) three 20.0 gm samples of active gel were mixed with the Erythromycin EtOH soln. for three minutes with a plastic spatula and allowed to rest for approximately 15 minutes.

A 1.0 gm sample in duplicate was removed from each of the three samples and mixed first with MeOH and then with 0,.1M pH 8.0 PO_4 buffer to a total volume of 200 ml. This mixture was blended on a blender at low speed for three minutes at room temperature. The solution was allowed to lose its foam layer by waiting five minutes and then a 1.0 ml sample was removed and Q.S.'d to 109 ml with 0.1M PO_4 pH 8.0 buffer.

This was placed in stainless steel cylinders that had been previously dropped on to seeded Agar plates. The 4 ml top seed layer contained 1.5 ml stocks of *S. lutea* at 25% light transmission in a 1:40 dilution of standardizing solution) per 100 ml of the Agar.

The plates also had appropriate reference standards of μg/ml Erythromycin solution in alternate cylinders.

The standard curve plates as well as test plates were incubated at 35°C for 18 hours. The cylinders were removed and zone sizes read and compared with standard zone sizes.

Results: After a six week period each of the benzoyl peroxide—erythromycin gel formulations had a satisfactory concentration of active components.

Example 8

(A) 536.0 mg of purified water were stirred and 15.0 mg of Carbopol 940 (a carboxyl vinyl polymer, acid form, of B.F. Goodrich Co.) were added to the water while stirring. Stirring of the mixture was continued for 45 minutes. Then 4.095 mg of sodium hydroxide in 4.91 ml of purified water was added thereto. Stirring of the mixture was continued for 10 minutes, whereupon 150.0 mg of ethyl alcohol, 0.50 mg of perfume and 0.50 mg of methyl salicylate were added. To the stirred mixture was then added a mixture comprising 210.0 mg of wet pack micronized benzoyl peroxide (50% benzoyl peroxide—50% water), 2.0 mg of dioctyl sodium sulphosuccinate and 41.0 mg of purified water. The mixture was stirred for 30 more minutes until a smooth and elegant gel mixture was obtained.

(B) Samples of gel formulation from Part A weighing approximately 20.0 gm were mixed with 0.5 gm of Erythromycin in 3.0 ml ethanol to yield a total weight of 22.87 gm and placed containers. Each gram of sample contained about 21.85 mg of Erythromycin. The resultant product was suitable for use in the treatment of acne.

Example 9

Following the procedure of Example 8, the following gel formation was prepared:

Benzoyl peroxide (micronized)	5.46% by weight
Erythromycin	2.00% by weight
Ethyl alcohol	44.10% by weight
Polyoxyethylene lauryl ether	6.00% by weight
Colloidal magnesium alumunium silicate	2.50% by weight
Hydroxypropylmethylcellulose	1.00% by weight
Citric acid	0.05% by weight
Dioctyl sodium sulphosuccinate	0.02% by weight
Water	Q.S.

The resultant product had good stability and was effective for use in the treatment of acne.

CLAIMS

1. A composition for the topical treatment of acne, which composition comprises, as active ingredients, a peroxide of an organic acid in a micronized form and an erythromycin compound which is erythromycin or a derivative thereof, the peroxide being pr sent in an amount of from about one-half to about thirty times by weight of the erythromycin compound.

2. A composition according to claim 1, wherein the peroxide is benzoyl peroxide or lauroyl peroxide.

3. A composition according to claim 1 or claim 2, wherein the erythromycin compound is erythromycin.

4. A composition according to claim 1 or claim 2, wherein the erythromycin compound is erythromycin stearate or glucoheptonate.

5. A composition according to any one of the preceding claims, wherein the peroxide is present in an amount of from about 1% to about 30% by weight of the composition.

6. A composition according to claim 5, wherein the amount of peroxide is from about 5% to about 10% by weight of composition.

7. A composition according to any one of the preceding claims,wherein the erythromycin compound is present in an amount of from about 0.5% to about 5% by weight of the composition.

8. A composition according to any one of the preceding claims, wherein the peroxide is present in an amount of from about 1 to about 5 times by weight of the erythromycin compound.

9. A composition according to any one of the preceding claims, wherein the peroxide has a particle size of less than about 150 microns.

10. A composition according to any one of the preceding claims, wherein the peroxide has a mean average particle size of less than about 35 microns.

11. A composition according to any one of the preceding claims which includes a pharmaceutically-acceptable diluent or carrier.

12. A composition according to claim 11, wherein the diluent or carrier is a solid and the composition is in the form of a powder.

13. A composition according to claim 11, wherein the diluent or carrier is semi-solid and the composition is in the form of a cream or ointment.

14. A composition according to claim 11, wherein the diluent or carrier is a liquid and the composition is in the form of a suspension or solution.

15. A composition according to claim 14, wherein the liquid diluent or carrier is water, methanol, ethanol and/or acetone.

16. A composition according to claim 11, wherein the diluent or carrier is a mixture of water, a lower alkyl alcohol and a gelling agent and the composition is in the form of a hydroalcoholic gel.

17. A composition according to any one of the preceding claims, which also includes dioctyl sodium sulphosuccinate as a stabilizing agent and surfactant.

18. A composition according to claim 17 wherein the amount of dioctyl sodium sulphosuccinate is from about 0.1% to about 6.0% by weight of composition.

19. A composition according to claim 17 or claim 18, which also includes from about 1.0% to about 6.0% by weight of another wetting agent.

20. A composition according to any one of claims 16 to 19, wherein the gelling agent is present in an amount of from about 0.5% to about 15% by weight of the composition.

21. A composition according to any one of claims 16 to 20, wherein the gelling agent is a colloidal magnesium aluminium silicate, hydroxypropylmethylcellulose, a microcrystalline cellulose or a hydroxylated vinylic polymer.

22. An aqueous alcoholic gel composition suitable for the treatment of acne comprising:
(a) from about 1% to about 30% by weight of micronized benzoyl peroxide having a particle size of less than about 150 microns with a mean average particle size of less than about 35 microns;
(b) from about 2.0% to about 5.0% by weight of an erythromycin or a derivative thereof;
(c) from about 0.1% to about 6.0% by weight of a dioctyl sodium sulphosuccinate;
(d) from about 1.0% to about 6.0% by weight of a further wetting agent;
(e) from about 0.5% to about 15% by weight of a gelling agent;
(f) from about 10% to about 80% of a lower alkyl alcohol; and
(g) water.

23. A two-part composition for the topical treatment of acne, which composition comprises: in a first part an erythromycin compound which is erythromycin or a derivative thereof, and in a second part an organic acid peroxide in a micronized form and a pharmaceutically-acc ptable diluent or carrier, the peroxide and the erythromycin compound being provided in a ratio whereby when the two parts are mixed the peroxide is present in an amount of from about one-half to about thirty times by weight of the erythromycin compound.

24. A two-part composition according to claim 23, wherein each part is formulated so that on mixing there is formed a composition according to any one of claims 2 to 22, all of the ingredients of the composition apart from the erythromycin compound and optionally any solvent therefor being provided by the second part of the composition.

25. A package for providing a composition according to any one of claims 1 to 22, which package comprises a first closable container having therein a said erythromycin compound and optionally a solvent therefor, and second closable container having therein a said organic acid peroxide together with any additional ingredients, the package including means to indicate or ensure that the contents of the containers are mixed in a ratio such that in the resulting mixture the amount of peroxide is from about one-half to about thirty times by weight of the erythromycin compound.

26. A composition according to claim 1 substantially as hereinbefore described with reference to or as derived from any one of the specific Examples.

27. A two-part composition according to claim 23 substantially as herinbefore described with reference to any one of Examples 3 to 8.

28. A package according to claim 25 substantially as hereinbefore described with reference to the accompanying drawings and/or any one of Examples 3 to 6.

29. For use in a method for treating acne in humans by providing on the affected skin area one or more topically active ingredients a combination of erythromycin or a derivative thereof and micronized peroxide of an organic acid.

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